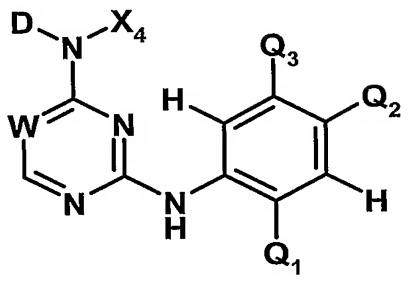
CLAIMS

We claim:

1. A method of treating cancer in a mammal, comprising: administering to said mammal

(a) a compound of formula I

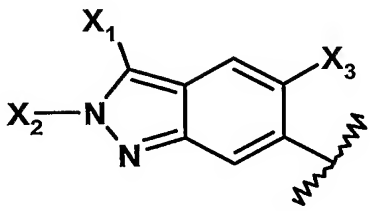


(I)

or a salt, solvate, or physiologically functional derivative thereof;

wherein:

D is



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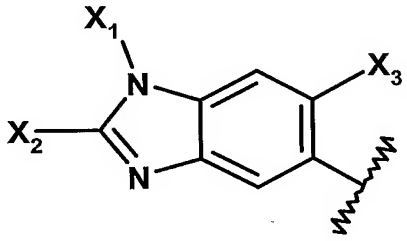
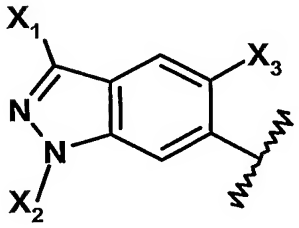


, or



;

X_1 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} hydroxyalkyl;

X_2 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $C(O)R^1$, or aralkyl;

X_3 is hydrogen or halogen;

X_4 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, heteroaralkyl, cyanoalkyl, $-(CH_2)_pC=CH(CH_2)_tH$, $-(CH_2)_pC\equiv C(CH_2)_tH$, or C_{3-7} cycloalkyl;

p is 1, 2, or 3;

t is 0 or 1;

W is N or C-R, wherein R is hydrogen, halogen, or cyano;

Q_1 is hydrogen, halogen, C_{1-2} haloalkyl, C_{1-2} alkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy;

Q_2 is A^1 or A^2;

Q_3 is A^1 when Q_2 is A^2 and Q_3 is A^2 when Q_2 is A^1;

wherein

A^1 is hydrogen, halogen, C_{1-3} alkyl, C_{1-3} haloalkyl, $-OR^1$, and

A^2 is the group defined by $-(Z)_m-(Z^1)-(Z^2)$, wherein

Z is CH_2 and m is 0, 1, 2, or 3, or

Z is NR^2 and m is 0 or 1, or

Z is oxygen and m is 0 or 1, or

Z is CH_2NR^2 and m is 0 or 1;

Z^1 is $S(O)_2$, S(O), or C(O); and

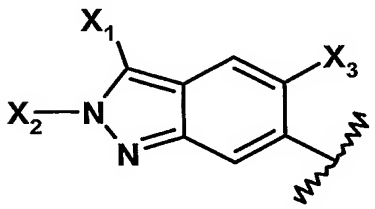
Z^2 is C_1-C_4 alkyl, NR^3R^4, aryl, arylamino, aralkyl, aralkoxy, or heteroaryl;

R^1 is C_{1-4} alkyl;

R^2, R^3, and R^4 are each independently selected from hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, $-S(O)_2R^5$, and $-C(O)R^5$;

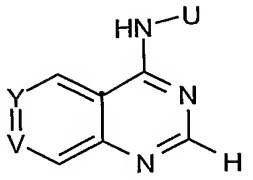
R^5 is C_{1-4} alkyl, or C_{3-7} cycloalkyl; and

when Z is oxygen then Z^1 is $S(O)_2$ and when D is



then X_2 is C_{1-4} alkyl, C_{1-4} haloalkyl, $C(O)R^1$, or aralkyl; and

(b) a compound of formula II



(II)

or a salt, solvate, or physiologically functional derivative thereof;

wherein

Y is CR^6 and V is N;

or Y is CR^6 and V is CR^7;

R^6 represents a group $CH_3SO_2CH_2CH_2NHCH_2$-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C_{1-4} alkyl or C_{1-4} alkoxy groups;

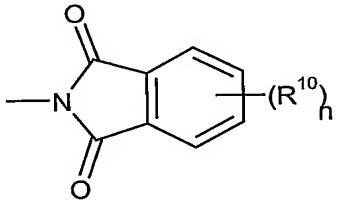
R^7 is selected from the group consisting of hydrogen, halo, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino and di[C_{1-4} alkyl]amino;

U represents a phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by an R^8 group and optionally substituted by at least one independently selected R^9 group;

R^8 is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R^8 represents trihalomethylbenzyl or trihalomethylbenzyloxy;

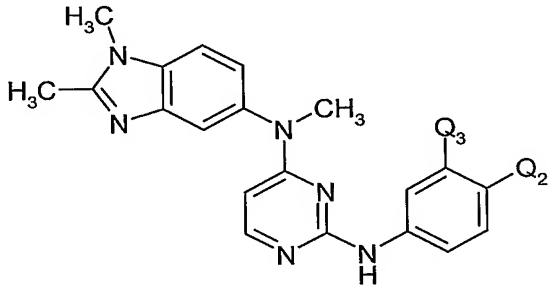
or R^8 represents a group of formula



wherein each R^{10} is independently selected from halogen, C_{1-4} alkyl and C_{1-4} alkoxy; and n is 0 to 3; and

each R^9 is independently hydroxy, halogen, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di[C_{1-4} alkyl]amino, C_{1-4} alkylthio, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, C_{1-4} alkylcarbonyl, carboxy, carbamoyl, C_{1-4} alkoxycarbonyl, C_{1-4} alkanoylamino, N-(C_{1-4} alkyl)carbamoyl, N,N-di(C_{1-4} alkyl) carbamoyl, cyano, nitro and trifluoromethyl.

2. The method of claim 1, wherein (a) the compound of formula I is a compound of formula I^a



$(I)^a$

or a salt, solvate or physiologically functional derivative thereof; wherein Q_3 is A^1 when Q_2 is A^2 and Q_3 is A^2 when Q_2 is A^1; wherein

A^1 is hydrogen, halogen, C_{1-3} alkyl, and

A^2 is the group defined by $-(Z)_m-(Z^1)-(Z^2)$, wherein

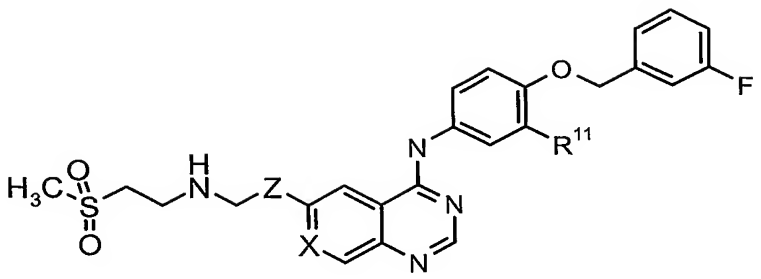
Z is CH_2 and m is 0, 1, 2, or 3;

Z^1 is $S(O)_2$, S(0), or C(O); and

Z^2 is C_{1-4} alkyl, or NR^3R^4;

R^3 and R^4 are each independently selected from hydrogen, or C_{1-4} alkyl; and

(b) the compound of formula II is a compound of formula II^a

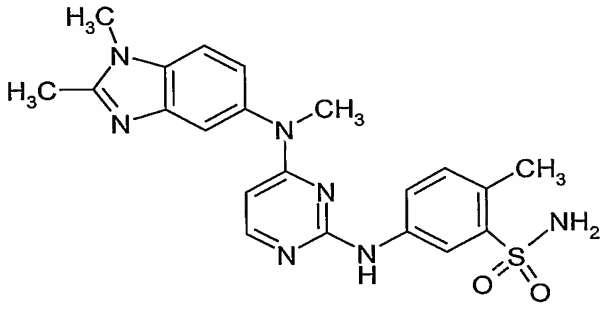


$(II)^a$

or a salt, solvate or physiologically functional derivative thereof;

wherein R^{11} is –Cl or –Br, X is CH , N, or CF, and Z is thiazole or furan.

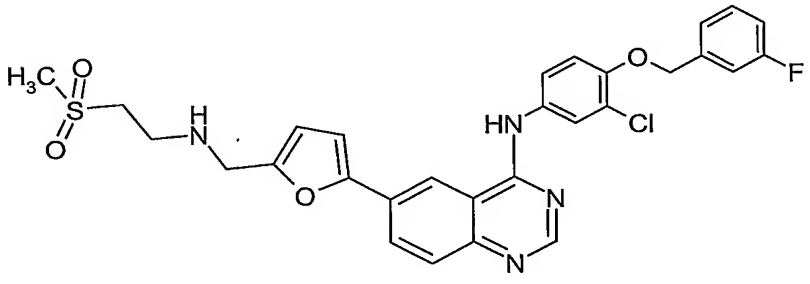
3. The method of claim 1, wherein (a) the compound of formula I is a compound of formula I^b



$(I)^b$

or a salt, solvate, or physiological functional derivative thereof; and

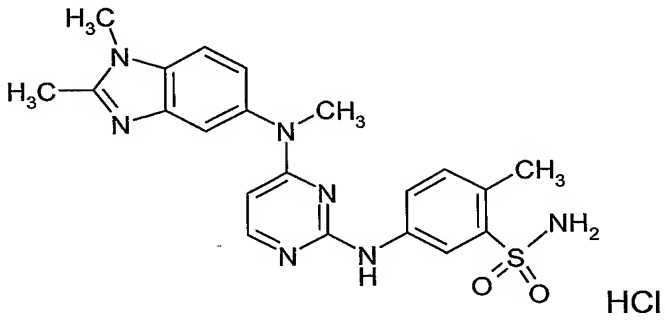
(b) the compound of formula II is a compound of formula II^b



$(II)^b$

or a salt, solvate, or physiological functional derivative thereof.

4. The method of claim 1, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I[b]

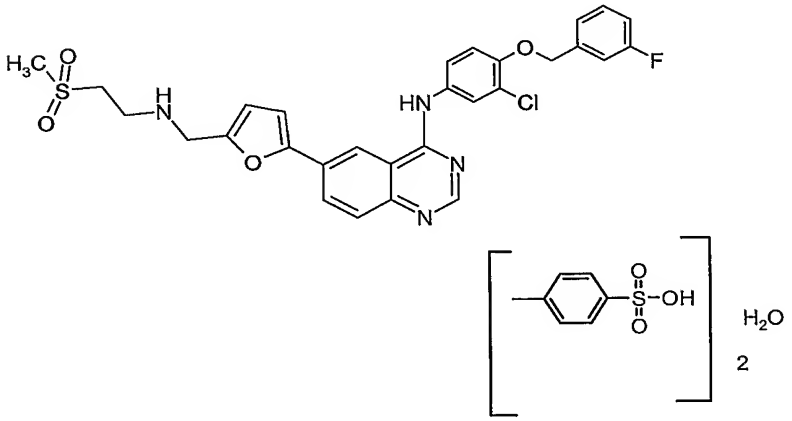


HCl

(I)[b]

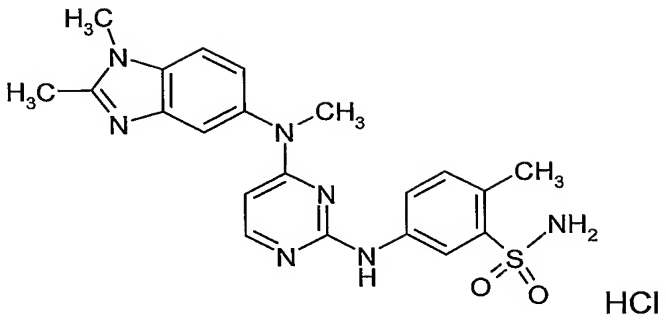
; and

(b) the compound of formula II is a monohydrate ditosylate salt of a compound of formula II[b]



(II)[b]

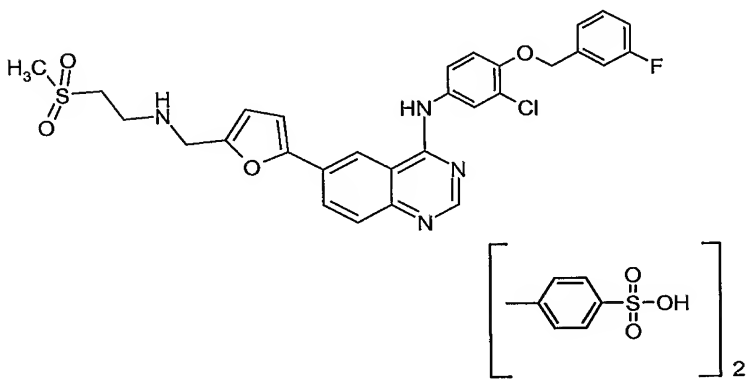
5. The method of claim 1, wherein the compound of formula I is a monohydrochloride salt of a compound of formula I[b]



(I)[b]

; and

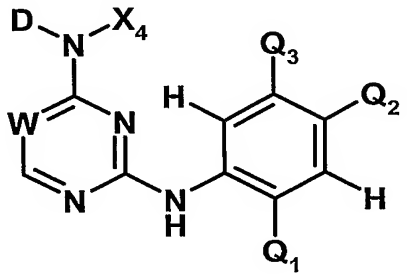
(b) the compound of formula II is an anhydrous ditosylate salt of a compound of formula II[b]



(II)[b]

6. A pharmaceutical composition comprising:

(a) a compound of formula I

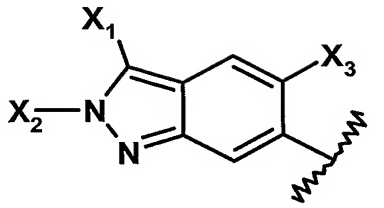


(I)

or a salt, solvate, or physiologically functional derivative thereof;

wherein:

D is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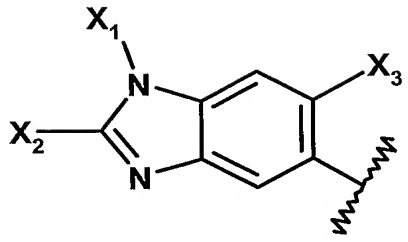
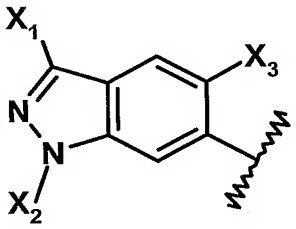

, or

;

X_1 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} hydroxyalkyl;

X_2 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $C(O)R^1$, or aralkyl;

X_3 is hydrogen or halogen;

X_4 is hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, heteroaralkyl, cyanoalkyl, $-(CH_2)_pC{=}CH(CH_2)_tH$, $-(CH_2)_pC{\equiv}C(CH_2)_tH$, or C_{3-7} cycloalkyl;

p is 1, 2, or 3;

t is 0 or 1;

W is N or C-R, wherein R is hydrogen, halogen, or cyano;

Q_1 is hydrogen, halogen, C_{1-2} haloalkyl, C_{1-2} alkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy;

Q_2 is A^1 or A^2;

Q_3 is A^1 when Q_2 is A^2 and Q_3 is A^2 when Q_2 is A^1;

wherein

A^1 is hydrogen, halogen, C_{1-3} alkyl, C_{1-3} haloalkyl, $-OR^1$, and

A^2 is the group defined by $-(Z)_m-(Z^1)-(Z^2)$, wherein

Z is CH_2 and m is 0, 1, 2, or 3, or

Z is NR^2 and m is 0 or 1, or

Z is oxygen and m is 0 or 1, or

Z is CH_2NR^2 and m is 0 or 1;

Z^1 is $S(O)_2$, S(O), or C(O); and

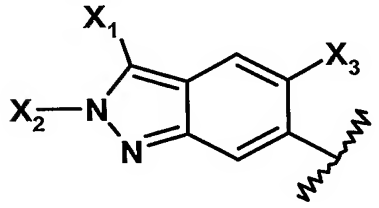
Z^2 is C_{1-4} alkyl, NR^3R^4, aryl, arylamino, aralkyl, aralkoxy, or heteroaryl;

R^1 is C_{1-4} alkyl;

R^2, R^3, and R^4 are each independently selected from hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, $-S(O)_2R^5$, and $-C(O)R^5$;

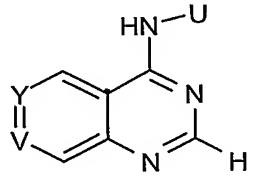
R^5 is C_{1-4} alkyl, or C_{3-7} cycloalkyl; and

when Z is oxygen then Z^1 is $S(O)_2$ and when D is



then X_2 is C_{1-4} alkyl, C_{1-4} haloalkyl, $C(O)R^1$, or aralkyl; and

(b) a compound of formula II



(II)

or a salt, solvate, or physiologically functional derivative thereof;

wherein

Y is CR^6 and V is N;

or Y is CR^6 and V is CR^7;

R^6 represents a group $CH_3SO_2CH_2CH_2NHCH_2$-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C_{1-4} alkyl or C_{1-4} alkoxy groups;

R^7 is selected from the group consisting of hydrogen, halo, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino and di[C_{1-4} alkyl]amino;

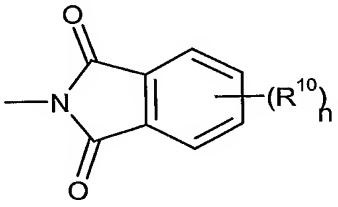
U represents a phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by an R^8

group and optionally substituted by at least one independently selected R^9 group;

R^8 is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R^8 represents trihalomethylbenzyl or trihalomethylbenzyloxy;

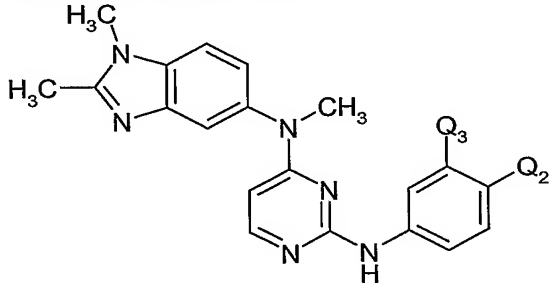
or R^8 represents a group of formula



wherein each R^{10} is independently selected from halogen, C_{1-4} alkyl and C_{1-4} alkoxy; and n is 0 to 3; and

each R^9 is independently hydroxy, halogen, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di[C_{1-4} alkyl]amino, C_{1-4} alkylthio, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, C_{1-4} alkylcarbonyl, carboxy, carbamoyl, C_{1-4} alkoxycarbonyl, C_{1-4} alkanoylamino, N-(C_{1-4} alkyl)carbamoyl, N,N-di(C_{1-4} alkyl)carbamoyl, cyano, nitro and trifluoromethyl.

7. The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a compound of formula I^a



$(I)^a$

or a salt, solvate or physiologically functional derivative thereof;

wherein Q_3 is A^1 when Q_2 is A^2 and Q_3 is A^2 when Q_2 is A^1;

wherein

A^1 is hydrogen, halogen, C_{1-3} alkyl, and

A^2 is the group defined by $-(Z)_m-(Z^1)-(Z^2)$, wherein

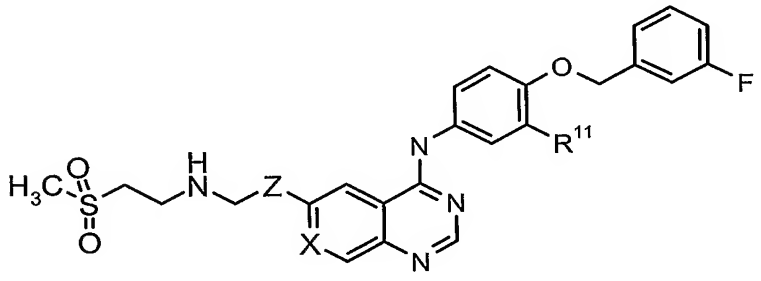
Z is CH_2 and m is 0, 1, 2, or 3;

Z^1 is $S(O)_2$, S(0), or C(O); and

Z^2 is C_{1-4} alkyl, or NR^3R^4;

R^3 and R^4 are each independently selected from hydrogen, or C_{1-4} alkyl; and

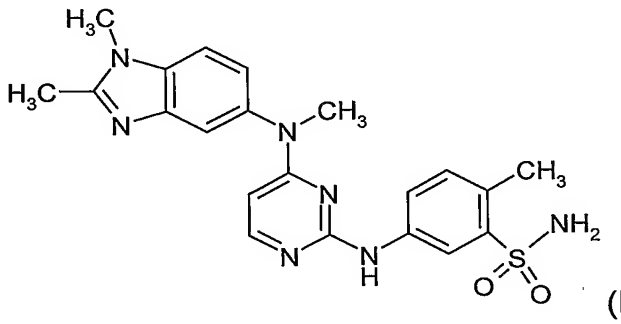
(b) the compound of formula II is a compound of formula II^a



$(II)^a$

or a salt, solvate or physiologically functional derivative thereof; wherein R^{11} is –Cl or –Br, X is CH , N, or CF, and Z is thiazole or furan.

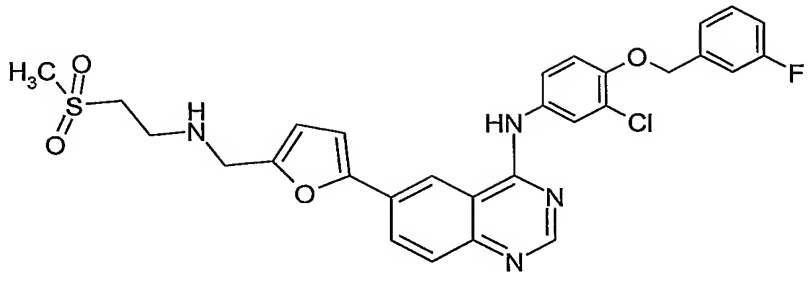
8. The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a compound of formula I^b



$(I)^b$

or a salt, solvate, or physiological functional derivative thereof; and

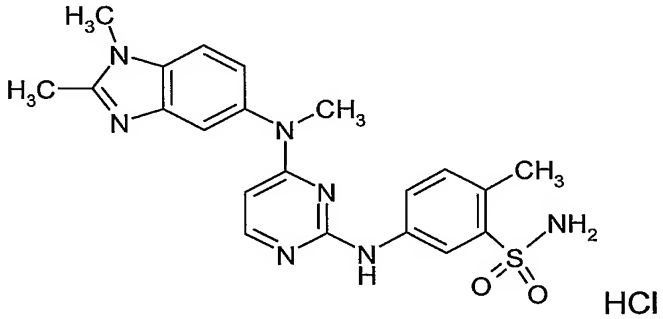
(b) the compound of formula II is a compound of formula II^b



(II)[b]

or a salt, solvate, or physiological functional derivative thereof.

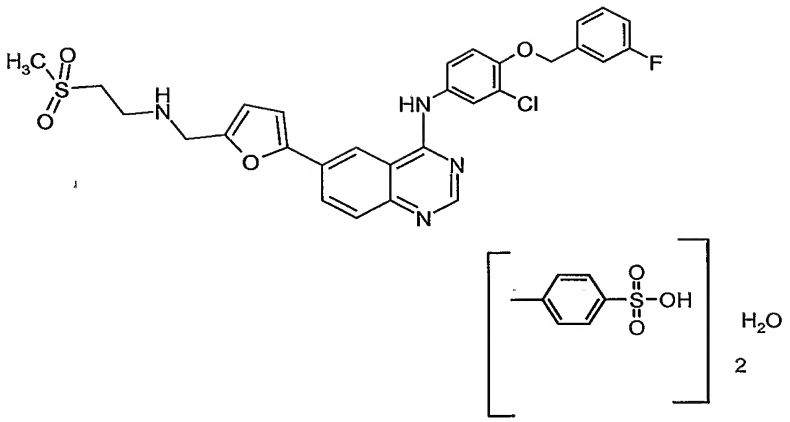
9. The pharmaceutical compostion of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I[b]



(I)[b]

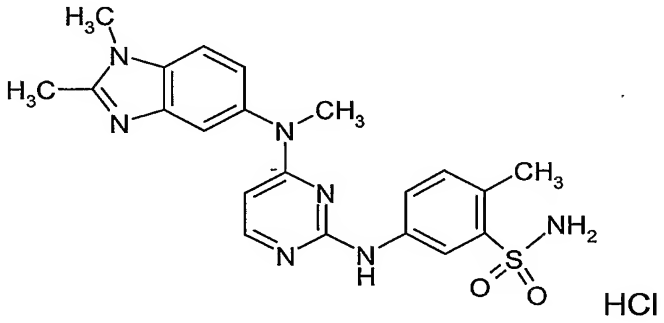
; and

(b) the compound of formula II is a monohydrate ditosylate salt of the compound of formula II[b]



(II)[b]

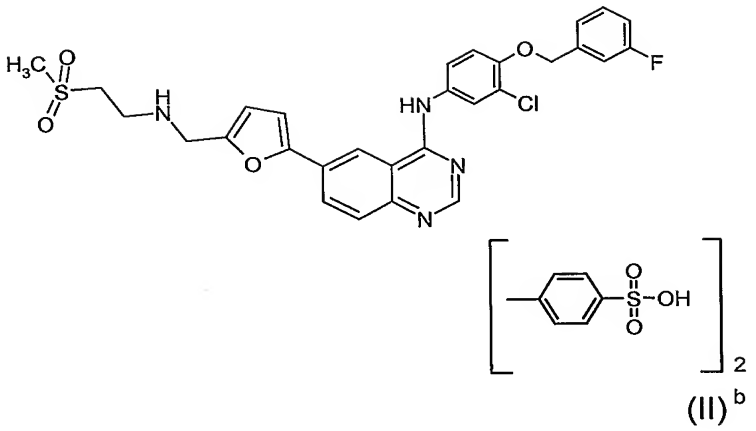
10. The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I[b]



(I)[b]

; and

(b) the compound of formula II is an anhydrous ditosylate salt of the compound of formula II[b]



(II)^b

11. A pharmaceutical combination comprising: a compound of formula I, I^a or I^b or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II^a or II^b or salt, solvate or physiologically functional derivative thereof for use in therapy.

12. The use of a pharmaceutical combination comprising: a compound of formula I, I^a or I^b or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II^a or II^b or salt, solvate or physiologically functional derivative thereof for the preparation of a medicament useful in the treatment of cancer.